Application Serial No. 09/560,475 Atty. Docket No. 028870-178

REMARKS

Claims 12 and 16-25 are now pending. Claim 12 was amended to more clearly recite local administration of a locally effective TNF-α lowering amount of bioactive glass particles with a size less than about 20 µm. No new matter was added.

Claims 12 and 16-25 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

Applicants first want to thank Examiner Pulliam and Examiner Kishore for the helpful interview April 2, 2003. Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 in support of the comments herein and in response to the discussion at the interview.

During the interview, the TNF-α response in various tissues was discussed. As set forth in the attached Declaration under 37 C.F.R. § 1.132 and the exhibits attached thereto, the reduction of TNF-α upon administration of bioactive glass particles as shown in Example 2 in the peritoneal cavity will take place at any site in the patient. In view thereof, the examples provided sufficiently enable the claims, as amended, directed to administering locally a locally effective TNF-α lowering amount of bioactive glass particles with a size less than about 20 microns.

The Bosetti et al. article cited in the Office Action was also discussed during the interview. Only an abstract of Bosetti et al. had been cited at the time of the interview. In order to obtain a more comprehensive understanding of the teachings of Bosetti et al., attached hereto is a complete copy of the article. A careful analysis of the Bosetti et al. article in its entirety confirms that the experiments conducted and described in Bosetti et al. do not provide any information relevant to the teachings of the present application and do not detract from the patentability of the present claims.

Bosetti et al. was cited, according to the Office Action, as a contradictory article which allegedly calls into question the enablement of the present specification. However, the teachings of Bosetti et al. are so different from the invention defined by the subject claims as to have no bearing on the enablement of the present application.

First, claim 12 is directed to a method for minimizing the production of TNF-α caused by an inflammatory response in a patient comprising locally administering a locally effective TNF-α lowering amount of bioactive glass paticles with a size less than about 20 microns to the patient. Bosetti et al., to the contrary, deals only with *in vitro* testing of particles from 90-700 microns and does not discuss production of TNF-α caused by an inflammatory response. Thus, Bosetti et al. is testing completely different materials in a completely different setting from the examples of the application which show the results of *in vivo* testing of bioactive glass particles with a size less than about 20 microns, as claimed.

Second, Bosetti et al. allowed the cells tested to incubate for three days prior to testing for TNF-α. As discussed in paragraph 6 of the attached Declaration under 37 C.F.R. § 1.132, however, particles of the size claimed would not exist in the body after three days. The effect of the claimed method is inherently transient since the small particles used are resorbed *in vivo*. *See, page 7 of the application* and "Bioglass® Attenuates a Proinflammatory Response in Mouse Peritoneal Endotoxicosis", *Shock*, 17(2): 135-138 (2002), *cited in Applicants' Amendment filed October 24, 2002*. Thus, the testing of Bosetti et al. of very large particles *in vitro* does not provide any illumination as to how particles of the size used in the invention will act *in vivo*. This information is adequately provided by the present specification. In view thereof, Applicants respectfully submit that Bosetti et al. would not be viewed by one of skill in the art as relevant to the invention as defined by the claims. Rather, the examples of the specification provide the needed enablement to carry out the claimed invention.

In view of the teachings of the specification and the examples provided which support the claims, Applicants submit that the claims would enable one of skill in the art to make and/or use the invention. Thus, Applicants respectfully request that the rejection under §112 be withdrawn.

Applicants believe they have responded to all matters raised in the above referenced Office Action and that the application is now in condition for allowance. If the Examiner has any questions concerning this Application or this Response and Amendment, she is invited to contact the undersigned.

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Respectfully submitted,
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